EXHIBIT 21

IMAGING OF THE DISEASES OF THE CHEST

FOURTH EDITION

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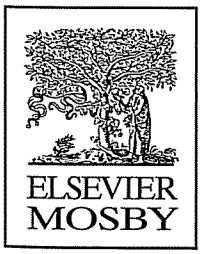

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Asbestos related diseases

Asbestos is composed of a group of fibrous silicates with differing chemical and physical properties but with the notable common property of heat resistance (Box 8.5). Chemical differences such as solubility and acid resistance, and physical differences such as fiber length, brittleness, and texture, are probably important determinants of the distribution and severity of deleterious effects on the lungs and pleura. Asbestos is divided into two principal subgroups based on the physical properties of the fibers: the serpentines; and the amphiboles. Serpentine asbestos has long, curly, flexible, smooth fibers composed of fibrillary subunits. The only serpentine asbestos used commercially is chrysotile, which accounts for >90% of the asbestos used in the United States today.[196] The amphiboles have straight, needlelike fibers of varying length, diameter, brittleness, and texture. The main types in use are crocidolite (blue asbestos), amosite (brown asbestos), tremolite, and anthophyllite. The longer, less soluble amphibole fibers tend to be very slow to clear from the lung, compared with chrysotile. A major reason for the decline in the use of the amphiboles was the recognition that the amphiboles, particularly crocidolite, have a much greater fibrogenic and carcinogenic potential than the serpentine form chrysotile.[197,198] It has even been suggested that chrysotile in its pure form has a minimal carcinogenic potential, and that contamination with the tremolite is the main reason for the carcinogenicity and fibrogenicity of the chrysotile forms of asbestos.[199–201] However, there is increasing evidence to support the contrary hypothesis that uncontaminated chrysotile is carcinogenic.[202–205]

***Box 8.5* Asbestos**

A family of naturally occurring fibrous silicates highly resistant to physical or chemical destruction

Two fiber types

Serpentine asbestos – long curly fibers composed of fibrillary subunits
- Chrysotile

Amphibole asbestos – straight shorter needlelike fibers
- Crocidolite
- Amosite
- Anthophyllite
- Tremolite

Uses
- Manufacture of cement, bricks, tiles, paints, fireproof felts and textiles
- Furnace and oven linings
- Insulation of steam pipes and electric lines
- Brake lining manufacture
- Fire proofing and insulation of buildings

World production and use of asbestos have expanded to an extraordinary degree over the past century. Production expanded from 50 tons per annum in the 1860s to a peak of >5 million tons per annum in the early 1970s.[206] Asbestos production has now declined somewhat as alternative materials have become available. Nevertheless, with the long latency which exists before the adverse effects of asbestos exposure become manifest (Box 8.6, Table 8.3), and with the vast tonnages of the material now in place or in use, asbestos is likely to remain one of the major environmental hazards well into the twenty-first century. A recent outbreak of asbestos related pleural disease and mesothelioma related to a vermiculite mine in Libby, Montana, illustrates the need for continued vigilance for asbestos related disease. The vermiculite was thought to be safe, but was contaminated with small amounts of tremolite, which was sufficient to cause a significant increase in mortality from lung cancer, mesothelioma, and asbestosis.[207,208]

***Box 8.6* Adverse effects of asbestos exposure**

Benign asbestos related pleural effusion(s)
Diffuse pleural thickening
Pleural plaque formation
Rounded atelectasis
Asbestosis
Malignancies
- Lung cancer and other epithelial malignancies – larynx, gastrointestinal tract
- Mesothelioma – pleural, peritoneal, pericardial

Benign asbestos related pleural effusion

Benign asbestos related pleural effusion is one of the less common manifestations of asbestos exposure, but it has the shortest latency period (Box 8.7).[209,210] The transient, often asymptomatic nature of these effusions and the lack of specific markers to indicate their cause undoubtedly accounted for the delayed recognition of this condition. Indeed the diagnosis is one of exclusion and should conform to the following criteria: (1) a history of occupational or environmental asbestos exposure; (2) no other cause for the effusion; and (3) no evidence of malignancy within 3 years of detecting the effusion.

In the noteworthy epidemiologic study by Epler et al,[209] the overall incidence of benign pleural effusion was 3.1%, with a 7% incidence among individuals having a heavy occupational exposure and a 0.2% incidence in environmentally exposed

Table 8.3 Frequency and latency of asbestos-related diseases (adapted with permission from Lynch et al. Imaging of diffuse lung disease. Hamilton: BC Decker, 2000)[a]

Finding	*Latency (years)*	*Approximate frequency in asbestos workers (%)*
Asbestos related effusion	5–20	3
Noncalcified plaques	15–30	15–80
Calcified plaques	30–40	10–50
Diffuse pleural thickening	10–40	10
Asbestosis	20–40	15–30
Lung cancer	>15	20–40[b]
Mesothelioma	15–40	10[b]

[a]The above figures are provided only as approximate guidelines. The prevalence or incidence of disease depends on the duration and intensity of exposure.
[b]Lifetime incidence.

***Box 8.7* Pleural changes related to asbestos exposure**

Benign asbestos related pleural effusion(s)
- May be the first manifestation of asbestos exposure
- Unilateral or bilateral
- Often asymptomatic; otherwise fever, pleuritic chest pain, or dyspnea
- Usually small but may be >500 ml
- Fluid – exudative often blood tinged
- Usually resolves completely but may leave diffuse pleural thickening

Diffuse pleural thickening
- Usually follows effusion
- Costophrenic sulcus blunted
- Usually asymptomatic but may cause pulmonary restriction

Pleural plaques
- Usually located on parietal pleura
- Most commonly seen between the fourth and eighth ribs
- No functional significance – they are a marker of asbestos exposure

Malignant mesothelioma

individuals. Effusions may be unilateral or bilateral and tend to recur. The amount of fluid is usually small; effusions >500 ml are uncommon. The fluid has the characteristics of an exudate and may be blood tinged. Symptoms include pleuritic pain, fever, and an elevated white blood cell count, but many patients have only mild symptoms or no symptoms at all. Indeed the presence of significant chest pain should lead to concern for mesothelioma.

Benign pleural effusion is the most common abnormality seen within 10 years of the onset of asbestos exposure. However, it may occur up to 58 years after initial exposure.[211] No direct causal relationship between benign effusions and the subsequent development of malignant pleural effusion has been postulated, but in one study of 70 cases of malignant mesothelioma,[212] five cases were preceded by what were regarded as successive benign pleural effusions for up to 7 years. In asbestos workers with pleural effusions, the diagnosis of benign effusion should be a diagnosis of exclusion.

Mesothelioma should be considered in any patient with a latency longer than 10 years, or in any patient with chest wall pain. In one series of 312 cases of mesothelioma, the latency periods ranged from 14 to 72 years with a mean of 48 years.[213] There appeared to be a relationship to the intensity of exposure with, for example, a mean latency period of 30 years for insulators as opposed to 52 years for domestically exposed women.

Benign pleural effusions are associated with the subsequent development of diffuse pleural thickening (Fig. 8.35).[214,215] McLoud et al[216] found that just over 50% of their patients with benign pleural effusions subsequently developed diffuse basal pleural thickening, an association also emphasized by Cookson et al.[217] As discussed later, there is a possible association between benign pleural effusions and the subsequent development of rounded atelectasis.[218] Diffuse pleural thickening frequently results in some restrictive impairment of pulmonary function.[219, 220] This is not usually progressive over time.[219,220] On rare occasion the degree and extent of the subsequent pleural thickening may be such that the resulting impairment of lung function necessitates surgical decortication.[120,221]

Asbestos related pleural plaques

Irregular pleural thickening and calcification were first positively related to exposure to asbestos in 1955,[218] and the occurrence of noncalcified, asbestos induced plaques was first reported in 1967.[222] Considerable attention has since been paid to these changes, as they represent the most frequent radiographic manifestation of exposure to asbestos. Although the incidence of pleural plaque formation increases with dose, the elapsed time from initial exposure is a more important factor.[223] Pleural

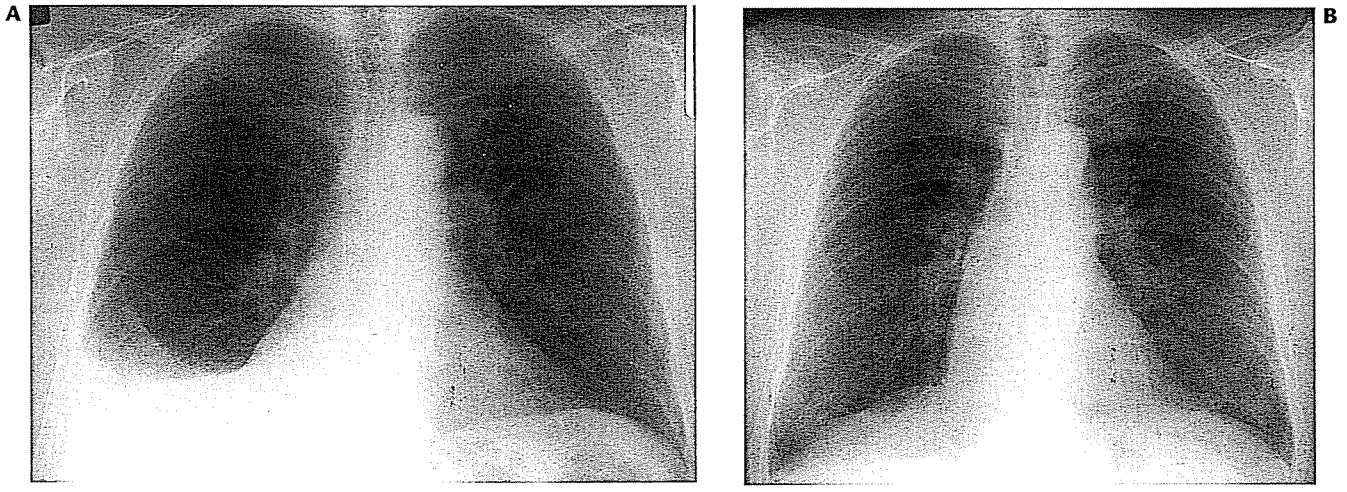

Fig. 8.35 Diffuse pleural thickening occurring as a sequel of benign asbestos related effusion. **A**, Chest radiograph shows an asymptomatic benign asbestos related effusion on the right. **B**, Chest radiograph 5 years later shows clearing of the effusion, but residual pleural thickening evident by blunting of the right costophrenic sulcus.

plaques are usually first identified >20–30 years after the initial asbestos exposure.[224] Asbestos induced pleural plaques occur on the parietal pleura, especially over the diaphragm and along the posterolateral chest wall. The apices, the costophrenic sulci, and the mediastinal surfaces tend to be spared. The plaques are composed of elevated areas of hyalinized fibrous tissue and frequently lie beneath the ribs. Although usually isolated, they may enlarge, spread, and coalesce. Dystrophic calcification within plaques is common and is more frequent as the plaques age and enlarge. Electron microscopy studies have identified asbestos fibers in the plaques on the parietal pleura, indicating that transpleural migration and assimilation of inhaled asbestos fibers must occur.[225] There is evidence that the widely used, more benign form of asbestos, chrysotile, is particularly associated with this transpleural migration, while the more fibrogenic and carcinogenic amphiboles, crocidolite and amosite, tend to be retained in the lung parenchyma.[224,226] This may account for the widespread finding of asbestos related pleural disease unassociated with parenchymal fibrosis or intrathoracic malignancy.

Population surveys in industrial regions and in asbestos mining areas have revealed a surprisingly high incidence of pleural plaques even in individuals who have only a remote connection with asbestos.[227–229] The use of asbestos is so widespread that many individuals are exposed unknowingly, and therefore accurate data are difficult to obtain. In autopsy based studies of unselected populations, pleural plaques may be found in up to 20% of patients, and a history of asbestos exposure is lacking in most of these,[230,231] particularly where the plaques are small or unilateral.[231] Therefore, the possibility of another, as yet unidentified, environmental agent as a cause of pleural plaque formation cannot be discounted. In an exhaustive study of pleural plaque formation in a rural region of Czechoslovakia, Rous and Studeny[232] were adamant that asbestos could not be implicated in their cases. Pleural plaque formation and calcification have been noted to occur after contact with other nonasbestos fibrous minerals, such as erionite in Turkey[233] and sepiolite in Bulgaria.[234]

On radiographic examination, noncalcified pleural plaques are irregular, smooth elevations of the pleura most easily identified in profile along the chest wall or over the diaphragm (Fig. 8.36). Plaques are less easily seen en face unless they are large or calcified. Plaques seen en face are seen as amorphous areas of increased density. They are relatively flat in relation to their width, and the density of the opacity projected over the lungs is therefore less than would be expected for a parenchymal lesion of equivalent size. Furthermore, one margin of the lesion is likely to be indistinct as it smooths off into normal pleura. Plaques are usually multiple and bilateral. Although Hu et al[235] reported that pleural plaques detected on chest radiographs

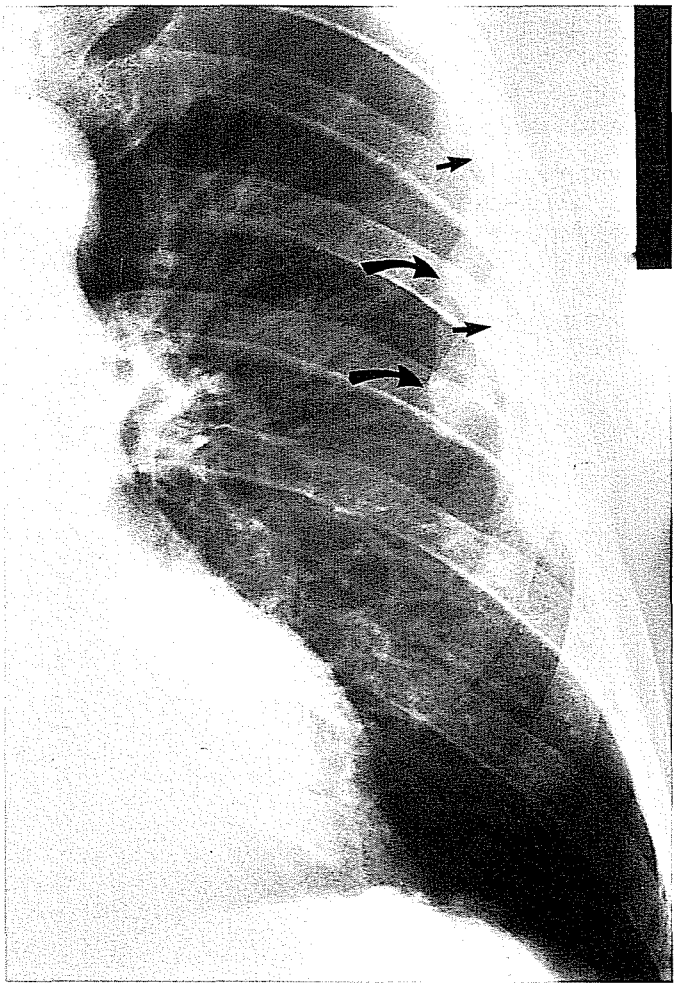

Fig. 8.36 Noncalcified pleural plaques seen in profile (straight arrows) and en face (curved arrows) in an asbestos exposed individual. Note the typical location between the fourth and eighth ribs, and the sparing of the costophrenic sulcus.

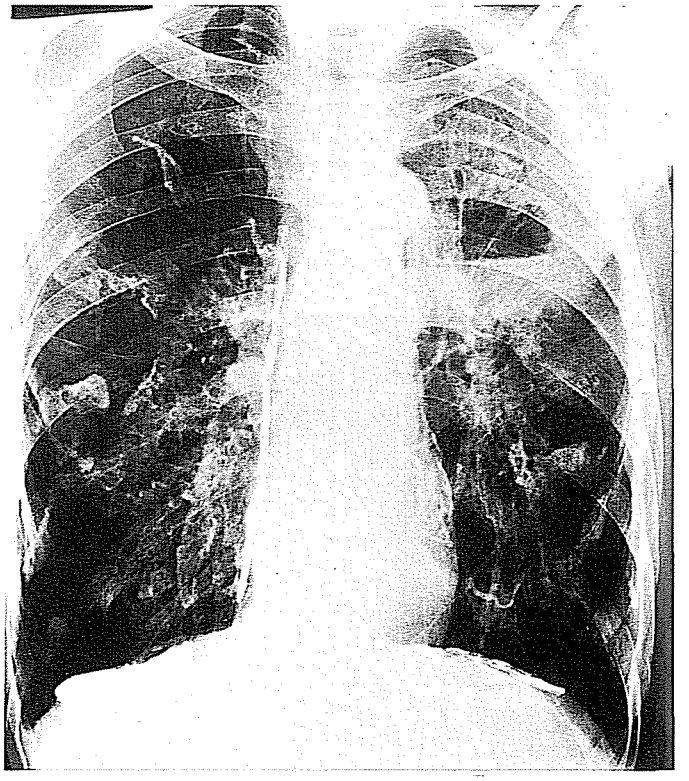

Fig. 8.37 Linear calcification in pleural plaques over the diaphragm and in the right paravertebral region. There is also calcified plaque formation seen en face, as well as a left upper lobe cavitating bronchial carcinoma.

were statistically more common on the left, a left-sided predominance was not confirmed in a CT based study.[236]

Calcification in pleural plaques is linear when seen in profile (Fig. 8.37), but when seen en face, its appearance is variable (Fig. 8.38), the most common type being "holly leaf" calcification (Fig. 8.39). Extensive pleural calcification in association with parenchymal fibrosis may be lacelike (Fig. 8.40). Enlargement and spreading of plaques result in thick irregular sheets of pleural thickening, which are often calcified. Pleural plaques may occur on the visceral pleura, but these can usually only be identified when a plaque is present in an interlobar fissure (Fig. 8.41).[237,238] Smooth visceral pleural thickening due to plaque must be distinguished from the more irregular subpleural fibrosis which occurs in patients with asbestosis.[239]

Asbestos exposure may be associated with pericardial fibrosis, with or without calcification or effusion.[240,241] Yazicioglu,[242] in a study of 511 cases of pleural disease secondary to environmental exposure to chrysolite asbestos in Turkey, found that 1.7% of cases had coincident pericardial calcification. Asbestos related pericardial fibrosis may lead to constrictive pericarditis.[240,243]

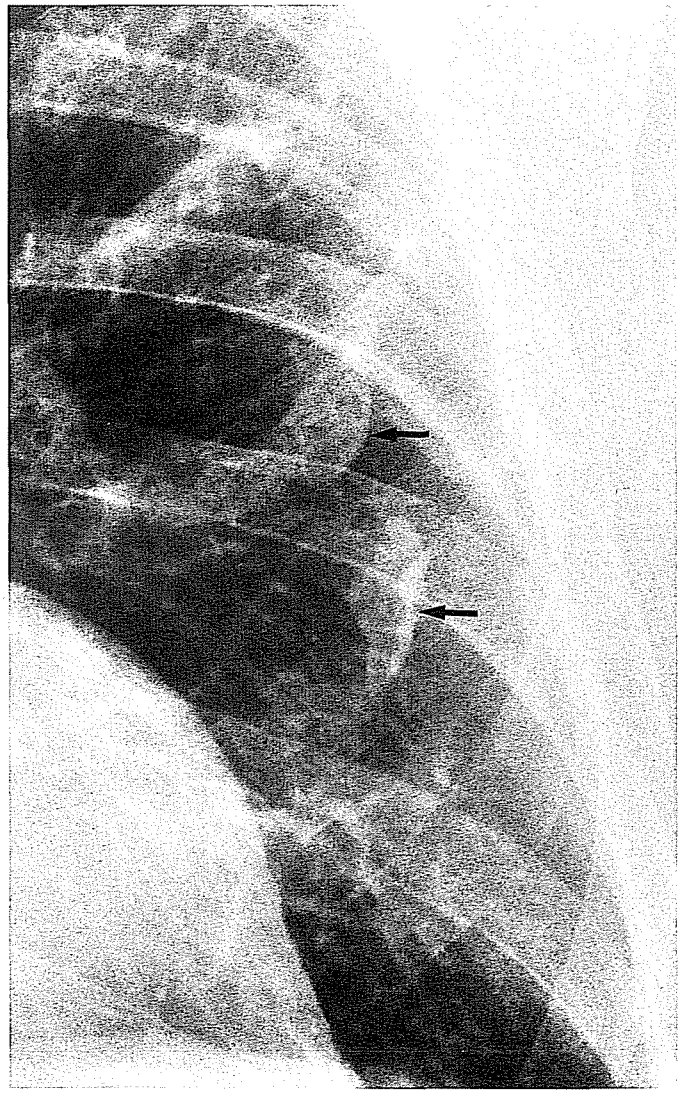

Fig. 8.38 Radiograph showing en face pleural calcifications (arrows).

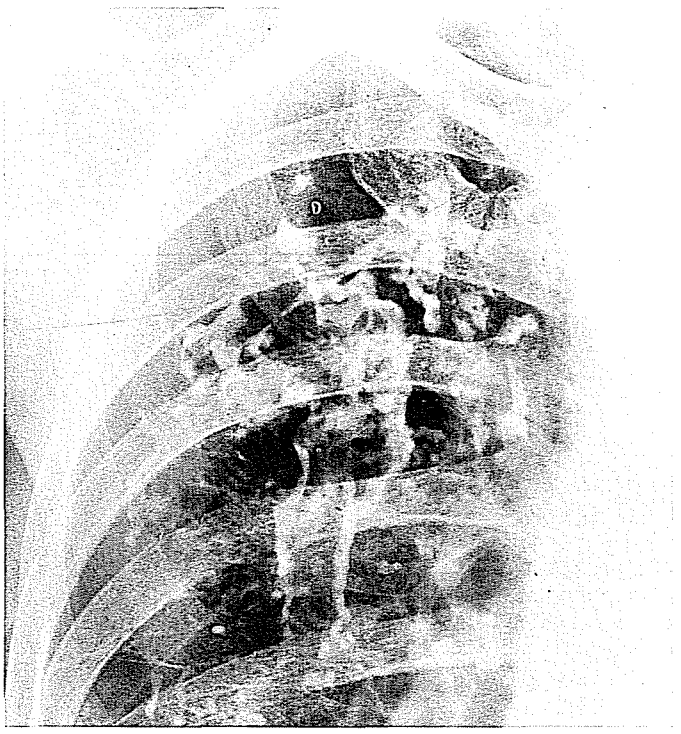

Fig. 8.39 "Holly leaf" calcification in asbestos related plaques seen en face.

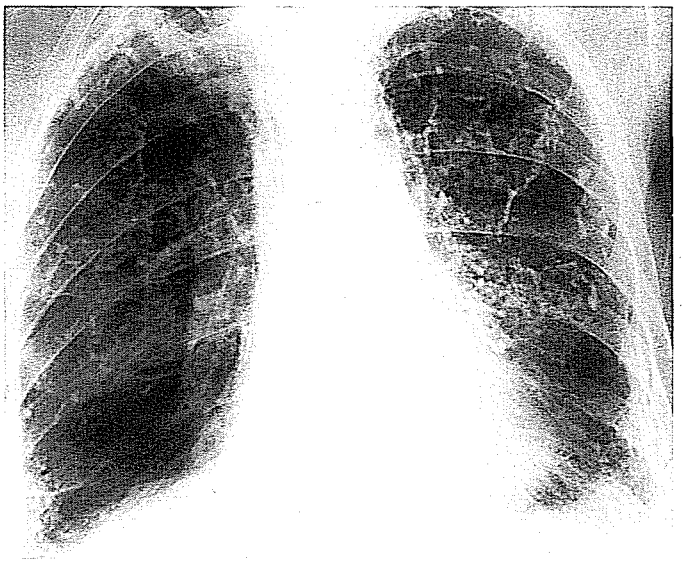

Fig. 8.40 Lacelike asbestos related pleural plaque formation seen en face.

Visualization of pleural plaques is improved by optimal radiographic technique. Oblique views can substantially increase the rate of plaque detection by throwing posterolateral plaques into profile.[244]

The differential diagnosis of pleural plaques includes extrapleural fat deposition in obesity,[245] extrapleural thickening in relation to multiple rib fractures, postinflammatory pleural thickening, and pleural metastases. In practice, the most frequent simulator of asbestos related pleural plaque formation is extra-

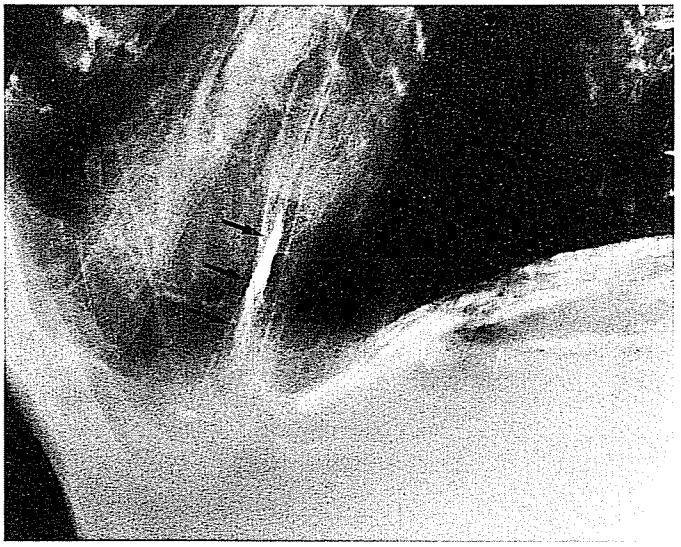

Fig. 8.41 Detail view of lateral chest radiograph shows calcified plaque formation in a major fissure (arrows). Calcification must be in the visceral pleura. There is also extensive diaphragmatic pleural calcification.

pleural fat deposition.[246] Extrapleural fat may be differentiated from pleural plaques by its lower density, its smooth, undulating outline, and by the fact that it typically extends all the way to the lung apices (Fig. 8.42). Fat is most abundant over the fourth to eighth ribs and does not involve the costophrenic sulci. Of course, CT will readily distinguish the soft tissue density of pleural plaques from extrapleural fat.

Although the presence of pleural plaques is associated with less physiologic impairment than diffuse pleural thickening, several studies have indicated that identification of plaques on chest radiographs is associated with evidence of pulmonary restriction, independent of the presence or extent of radiographic parenchymal abnormality.[220,247–250] However, it seems likely that at least some of this association is explained by the presence of subradiographic asbestosis.[251,252]

CT is substantially more sensitive than the chest radiograph for detection of pleural plaques (Fig. 8.43).[253–256] Contiguous CT imaging maximizes sensitivity for plaques.[257] CT is also more sensitive than radiographs for detecting calcification in plaques.[258] Elevated plaques may indent the adjacent lung, and may even cause ground-glass abnormality by interfering with local pulmonary expansion. Thinner plaques may be difficult to distinguish from the intercostal musculature, but may be identified by recognizing that they overlay ribs as well as intercostal spaces (Fig. 8.44).

Diffuse pleural thickening

It is important to distinguish between asbestos related diffuse pleural thickening and pleural plaques because patients with diffuse pleural thickening commonly have significant impairment of pulmonary function. The radiographic definition of diffuse pleural thickening has varied. The ILO classification defines it as pleural thickening that involves the costophrenic sulci (Figs 8.35 and 8.45),[105] while McLoud et al[216] also included patients in whom pleural plaques occupied more than one-quarter of the chest wall. Most studies have used the more restrictive ILO definition. On CT scanning, the definition of diffuse pleural thickening has also varied. Lynch et al[239] defined it as an area of pleural thickening >3 mm thick, >5 cm in transverse dimension, and >8 cm in craniocaudal dimension.[239] However, Copley et al[259] defined diffuse pleural thickening as pleural thickening with tapered margins, in contrast to pleural plaques, which were required by this definition to have well-defined margins. Since diffuse pleural thickening, by all definitions, is associated with physiologic impairment, it seems likely that the precise definition of this entity is of little importance.

Asbestos related diffuse pleural thickening must be distinguished from the visceral pleural and subpleural fibrosis which occurs in patients with many forms of lung fibrosis (including

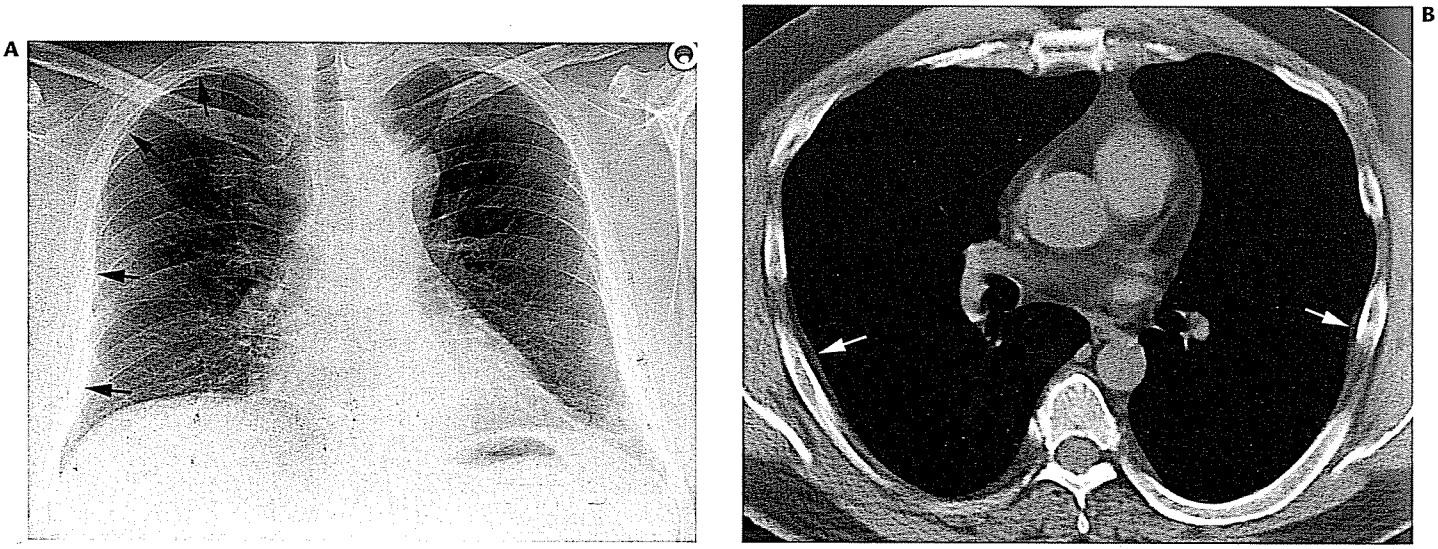

Fig. 8.42 Extrapleural fat. **A**, Chest radiograph shows soft tissue thickening extending in an undulating fashion all the way to the apices (arrows). The costophrenic sulci are not involved. **B**, CT confirms extrapleural fat (arrows).

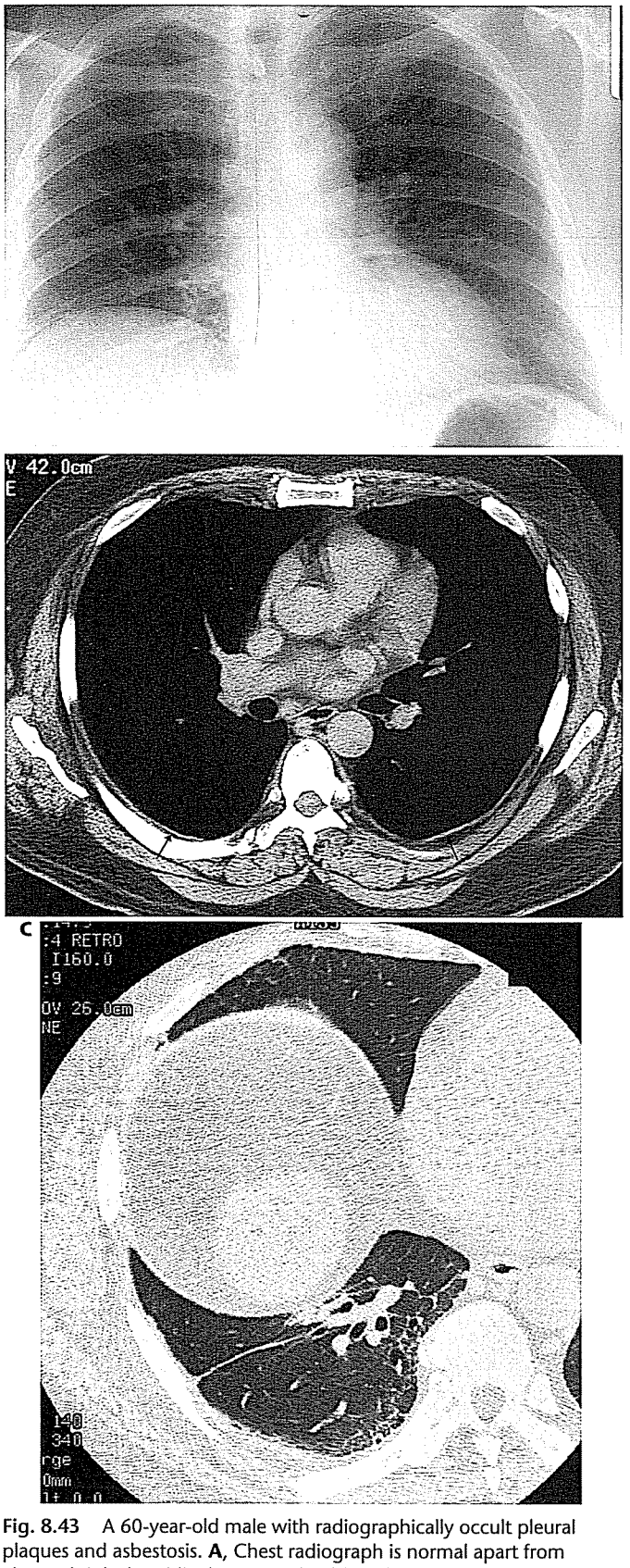

Fig. 8.43 A 60-year-old male with radiographically occult pleural plaques and asbestosis. **A**, Chest radiograph is normal apart from elevated right hemidiaphragm and mild cardiomegaly. **B**, CT shows pleural plaques (arrows) which are not visible on the chest radiograph because they are posterior. **C**, Supine HRCT shows fine parenchymal reticular abnormality with traction bronchiectasis. Septal thickening is seen in the nondependent anterior right lung.

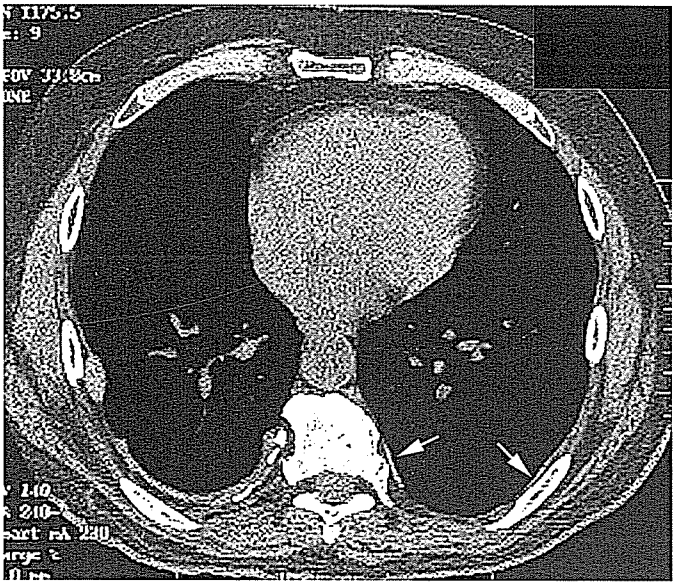

Fig. 8.44 A 68-year-old man with asbestos related pleural plaques. CT shows bilateral plaques. The plaques on the right are easy to recognize because they are elevated and the more medial plaque is partly calcified. The linear plaques on the left (arrows) are more subtle; the more medial plaque is recognizable because it is hyperdense, while the more lateral plaque is distinguishable from intercostal muscles because it overlies a rib.

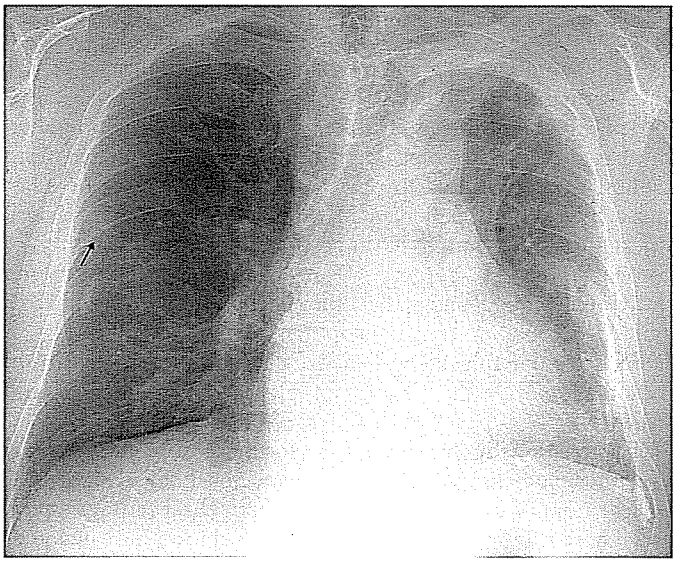

Fig. 8.45 Diffuse pleural thickening. Chest radiograph shows diffuse pleural thickening around the left hemithorax, associated with calcification, and blunting of the costophrenic sulcus. A noncalcified plaque is seen en face on the right (arrow).

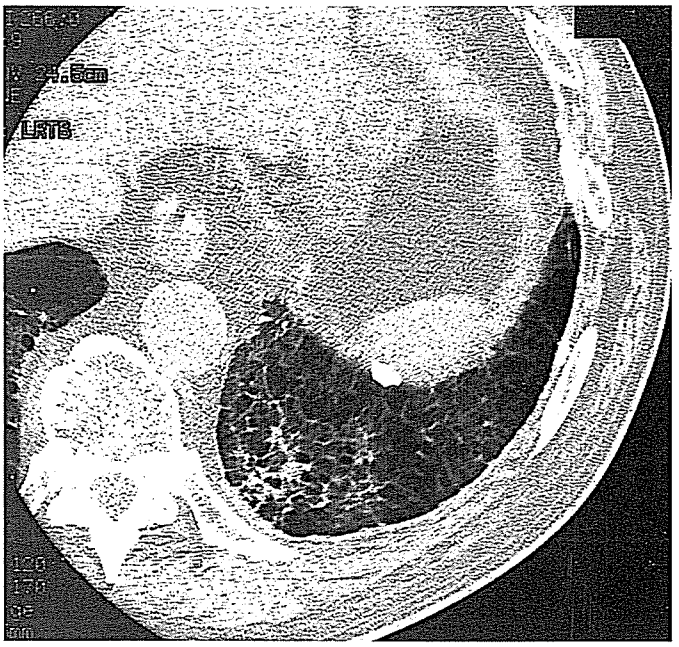

Fig. 8.46 Visceral pleural thickening in asbestosis. HRCT shows reticular abnormality with traction bronchiectasis. Note the fine irregularity of the visceral pleura, which differs from the smooth interface seen with parietal pleural plaques.

asbestosis). Pure parietal pleural thickening is usually sharply defined on CT, while visceral pleural fibrosis is associated with fine fibrous strands extending into the underlying lung, giving a "blurred" or "fluffy" demarcation to the pleural process (Fig. 8.46).[239,260] Visceral pleural fibrosis is usually, but not always, associated with other evidence of lung fibrosis. Visceral pleural/subpleural fibrosis can sometimes be identified on the chest radiograph as thickening of the interlobar fissures (scored as "pi" in the ILO classification system).[261] Asbestos related diffuse pleural thickening often cannot be differentiated from pleural thickening due to prior empyema, infection, or other cause. Interestingly, patients with asbestos related diffuse pleural thickening were found to have a more frequent history of coronary bypass surgery than other asbestos exposed individuals, suggesting that thoracic surgery may have a synergistic role in the development of this complication.[262] Diffuse pleural thickening can usually be differentiated from mesothelioma by the absence of pleural effusion or pleural masses.

The relationship between asbestos related pleural disease and physiologic impairment has been extensively evaluated. It is clear from numerous studies using both chest radiographs[220] and chest CT[259,262] that diffuse pleural thickening, however defined, is associated with substantial restriction of pulmonary function.

Rounded atelectasis

Rounded atelectasis, also called folded lung,[263] is a masslike area of lung collapse occurring in relation to an area of pleural thickening. The condition is not unique to asbestos related pleural thickening, and may also be seen with any other cause of exudative or organizing pleural disease. Although typically associated with benign pleural disease, it may sometimes be seen with mesothelioma.[264]

Hanke and Kretzschmar[265] proposed that rounded atelectasis occurs when an atelectatic area of lung becomes infolded during resorption of a pleural effusion. Other authors,[266,267] noting that rounded atelectasis is not always preceded by a pleural effusion, have suggested that it may result from centripetal contraction of a focus of visceral pleural fibrosis, causing buckling of the pleura and collapse of the underlying lung parenchyma.

The radiographic findings are characteristic (Box 8.8, Fig. 8.47). Rounded atelectasis typically presents with a masslike area adjacent to the pleura. Despite its name, rounded atelectasis is not usually round, but may be oval, lenticular, or irregular in shape. Acute angles are usually visible at the pleural margins and indicate an intraparenchymal location. The mass is usually separated from the diaphragm by interposed lung. The pleura is thickened, particularly in the vicinity of the lesion, and the costophrenic sulci are usually blunted or obliterated. The pathognomonic feature, however, is the characteristic pattern of distortion of the vessels and bronchi in the vicinity of the lesion. The vessels leading toward the mass are crowded, but as they reach the mass, they tend to arc around the undersurface of the mass before merging with it. This appearance has been described as the "comet tail" sign.[268] Rounded atelectasis may be solitary or multiple,[268] and is most commonly found in one of the lower lobes posteriorly or posteromedially.[269] The lingula or the middle lobe may also be involved (Fig. 8.48), but upper lobe involvement is less common.[266,270]

***Box 8.8* Rounded atelectasis**

Causes
Asbestos related pleural fibrosis (70%)
Tuberculous pleuritis or any nonspecific pleuritis
Dressler syndrome or chronic heart failure

Radiographic features
Intraparenchymal mass
Single or multiple
Juxtapleural location, often posterior and basal
Subjacent pleural thickening
Convergence of bronchovascular bundles into the mass – "comet tail"
Stability over time

CT features
Mass directly related to pleural thickening
Curving of bronchi and vessels into medial, lateral, and inferior aspects of mass
Homogeneous enhancement
Lobar volume loss (fissural displacement)

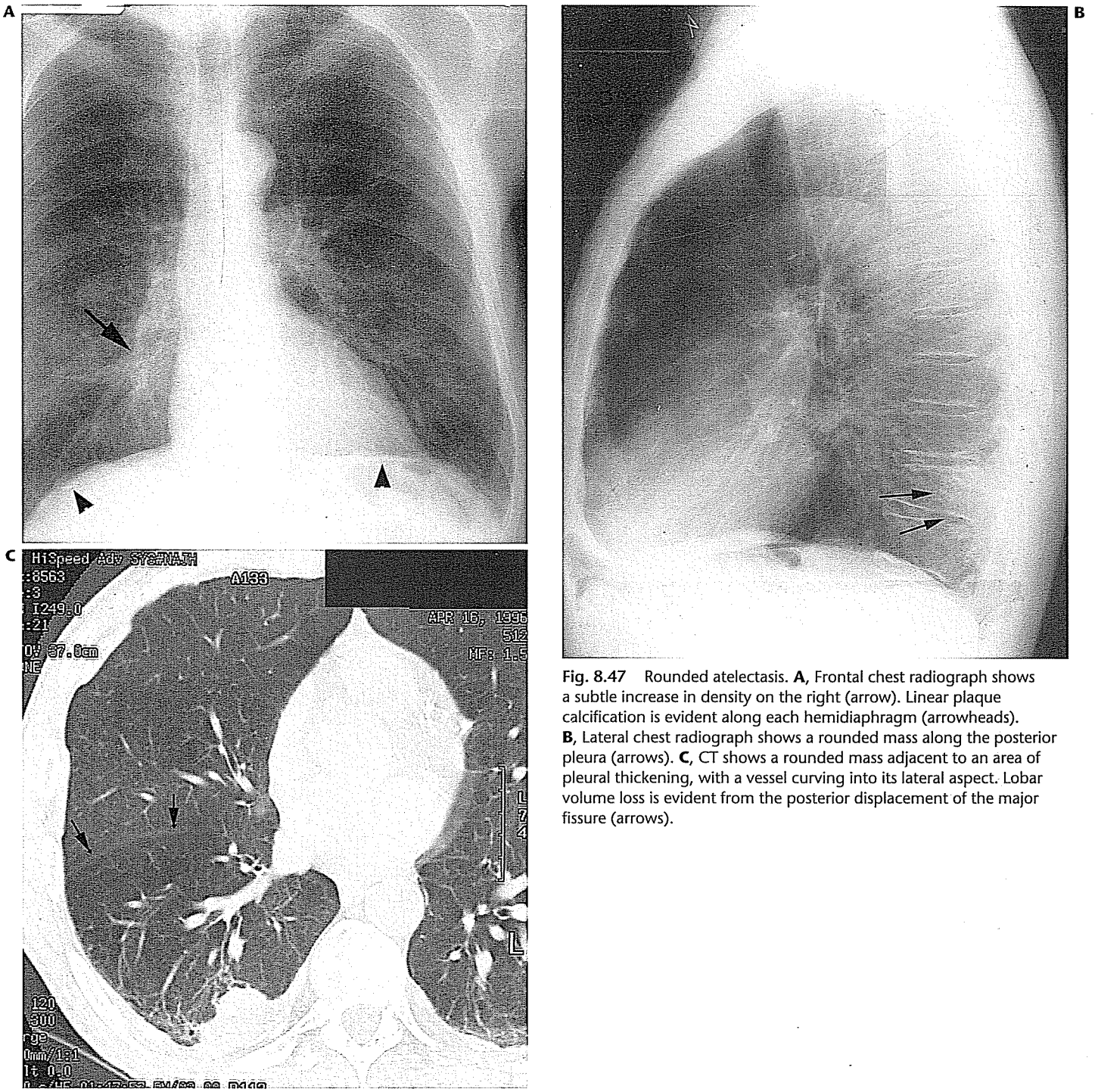

Fig. 8.47 Rounded atelectasis. **A**, Frontal chest radiograph shows a subtle increase in density on the right (arrow). Linear plaque calcification is evident along each hemidiaphragm (arrowheads). **B**, Lateral chest radiograph shows a rounded mass along the posterior pleura (arrows). **C**, CT shows a rounded mass adjacent to an area of pleural thickening, with a vessel curving into its lateral aspect. Lobar volume loss is evident from the posterior displacement of the major fissure (arrows).

CT is usually employed to confirm the diagnosis of rounded atelectasis. The characteristic CT signs of rounded atelectasis are the direct relationship of the mass to an area of pleural thickening, the presence of lobar volume loss with fissural displacement, and the curving of bronchi and vessels into the medial and lateral aspects of the mass (Fig. 8.49).[270–273] The margin directed toward the hilum is usually indistinct, though the other margins are well defined. An air bronchogram may be noted in the lesion. Like most types of atelectasis, rounded atelectasis enhances homogeneously after intravenous

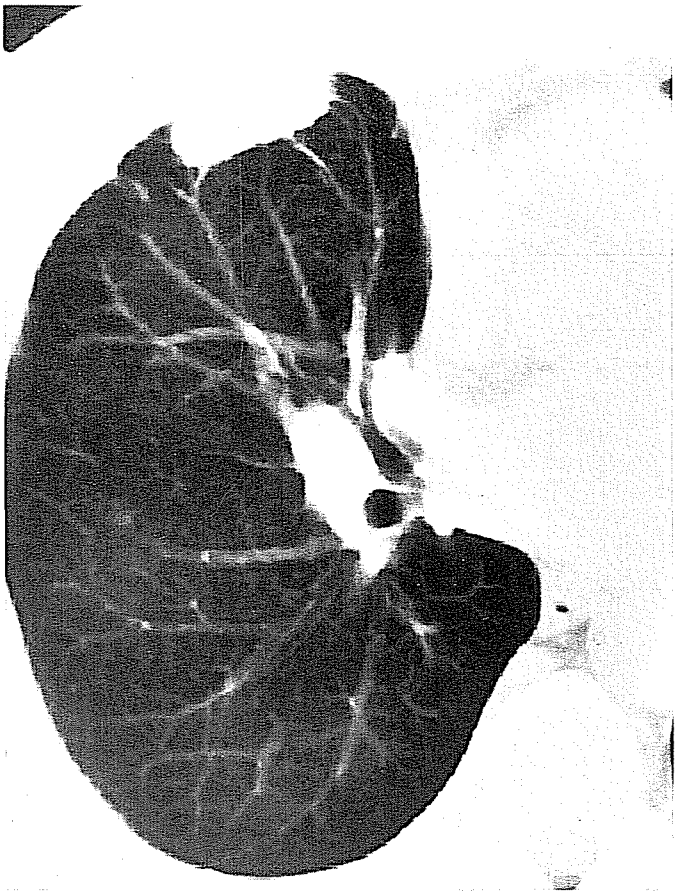

Fig. 8.48 Rounded atelectasis in the middle lobe of a middle-aged man with a previous asbestos related pleural effusion.

administration of contrast material.[274] Multiplanar reconstruction can provide an excellent depiction of the converging bronchovascular pattern (Fig. 8.50).

The appearance of rounded atelectasis on MRI has been described.[275] The lesion had a signal intensity similar to liver on T1-weighted images, and blood vessels and bronchi were seen to curve into the mass. On ultrasound, Marchbank et al[276] were able to identify a highly echogenic line extending into the mass from the pleural surface in 12 of 14 patients. These authors postulated that this line represented the scarred invaginated pleura.

The main differential diagnosis of rounded atelectasis is peripheral bronchogenic carcinoma, and biopsy may be necessary to exclude bronchogenic carcinoma where the CT features are atypical for rounded atelectasis. The necessity for continued follow up of cases of rounded atelectasis should be emphasized. Rounded atelectasis is ordinarily a static or very slowly growing process. O'Donovan et al,[277] in an evaluation of the reliability of CT in distinguishing rounded atelectasis from other pleural based masses, found that no single CT feature allowed perfect discrimination. They found the convergence of bronchovascular markings to be the best discriminator, but one case was encountered in which lung cancer developed within an area of rounded atelectasis.

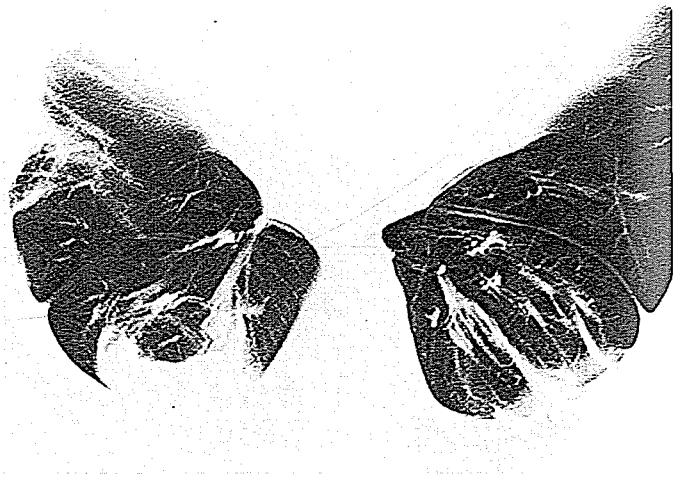

Fig. 8.49 CT in the prone position (but oriented as if supine) showing bilateral posterior basal rounded atelectasis. Note the marked bilateral posterior fissural displacement.

Asbestosis

Asbestosis is one of the main health hazards related to asbestos exposure, second only to bronchogenic carcinoma.[221] It was first identified with certainty at the turn of the century,[278] and by the mid 1980s an estimated 65,000 individuals in the United States had clinically diagnosable asbestosis.[279] The term "asbestosis" is generally reserved for asbestos induced pulmonary fibrosis (Box 8.9). Pleural abnormalities are excluded by definition, being regarded more as an indication of such exposure than as a significant disease entity. Asbestosis is related to the cumulative dust exposure whereas the parietal pleural changes are more related to the length of time since the initial exposure.[196] The time interval between the initial exposure and the development of evidence of asbestosis is extremely variable, but 20–30 years is usual. Intense exposures can cause asbestosis in as short a period as 3 years, but this is exceptional. The most fibrogenic form of asbestos is crocidolite, and in descending order of fibrogenicity are amosite, anthophyllite, and chrysotile.

***Box 8.9* Asbestosis**

Pulmonary fibrosis related to asbestos exposure

Chest radiograph
Small irregular opacities with basal and subpleural predominance
Benign asbestos related pleural changes and rounded atelectasis may be present

Computed tomography
Prone imaging is essential to detect early changes
Peripheral, basal, and posterior predominance
Interlobular septal thickening
Centrilobular thickening
Reticular abnormality
Honeycombing
Subpleural curvilinear density

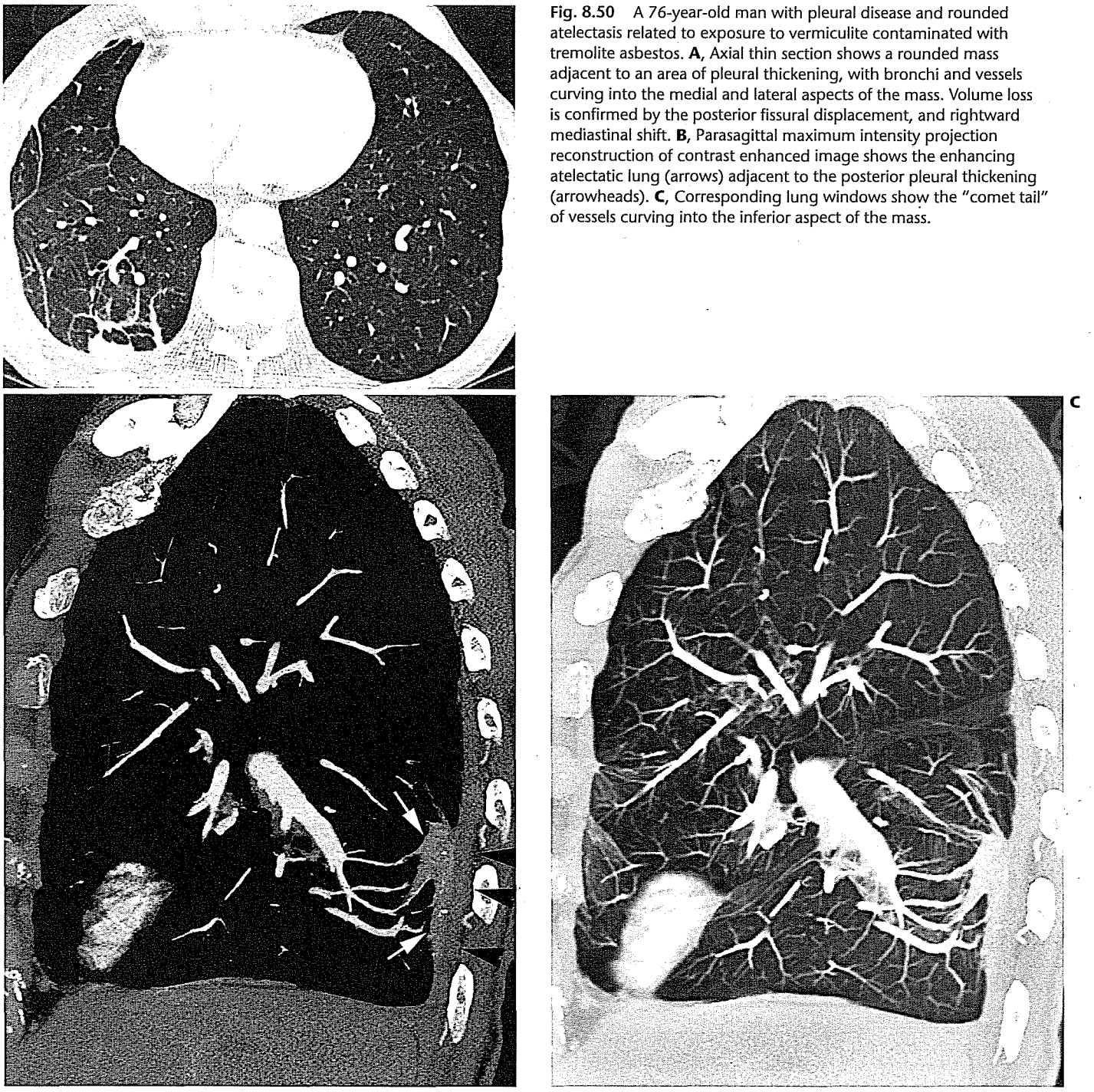

Fig. 8.50 A 76-year-old man with pleural disease and rounded atelectasis related to exposure to vermiculite contaminated with tremolite asbestos. **A**, Axial thin section shows a rounded mass adjacent to an area of pleural thickening, with bronchi and vessels curving into the medial and lateral aspects of the mass. Volume loss is confirmed by the posterior fissural displacement, and rightward mediastinal shift. **B**, Parasagittal maximum intensity projection reconstruction of contrast enhanced image shows the enhancing atelectatic lung (arrows) adjacent to the posterior pleural thickening (arrowheads). **C**, Corresponding lung windows show the "comet tail" of vessels curving into the inferior aspect of the mass.

Asbestos causes interstitial pulmonary fibrosis, spreading centrifugally from the region of the terminal bronchioles and the alveolar ducts,[280] with histologic features that are indistinguishable from those of IPF. The changes predominate in the subpleural portions of the lungs and at the lung bases. Visceral pleural thickening occurs, particularly over the regions of maximum fibrosis. Established asbestos induced pulmonary fibrosis tends to progress with time even after cessation of exposure.[281–283] Symptoms of dyspnea and dry cough usually develop approximately 20 years following initial exposure. Characteristic functional abnormalities consist of progressive reduction of both vital capacity and diffusing capacity.[221]

The diagnosis of asbestosis must not be based on imaging features alone. It requires consideration of the occupational history or possible environmental exposure, the clinical features (breathlessness, clubbing, lung crackles), the results of pulmonary function tests, and the chest radiographic and CT appearances.

On the chest radiograph, asbestosis typically presents with basal predominant reticular interstitial abnormality (small irregular opacities according to the ILO classification), which may later extend up the lateral chest wall (Figs 8.51 and 8.52). Progressive disease leads to honeycombing and lower lobe volume loss. Associated pleural abnormalities facilitate the diagnosis, but may be absent on the chest radiograph in 10% of cases.[284] Coarse or fine linear bands of fibrosis are commonly seen radiating from pleural surfaces. Conglomerate opacities akin to PMF have been reported in asbestosis,[285,286] but may relate to concomitant exposure to silica or talc.[287] A limitation of chest radiographic assessment of asbestosis is the questionable physiologic and pathologic significance of the small irregular opacities which are the chest radiographic hallmark of early asbestosis. In at least some cases these small irregular opacities appear to be related to a combination of cigarette smoke and asbestos exposure.[125]

The main indications for the use of CT in asbestosis are: (1) identification of pulmonary fibrosis as distinct from emphysema or diffuse pleural disease[254]; (2) identification of asbestosis in workers with normal parenchyma on chest radiographs[256,288]; (3) identification of pulmonary fibrosis for compensation purposes when the chest radiographs and pulmonary function tests give conflicting results; and (4) investigation of suspected pleural or parenchymal masses and guidance for their biopsy.

Early asbestosis is manifested on HRCT by prominent centrilobular structures, interlobular septal thickening, intralobular lines, curvilinear subpleural lines, and peripheral reticular opacities (Fig. 8.53).[253,256] Because of the posterior and basal predominance of the lesions of early asbestosis, examination of the lung bases in the prone position is critical for confirming the fixed nature of septal thickening and curvilinear subpleural lines. More advanced asbestosis is characterized by parenchymal bands of fibrosis, honeycombing, and traction bronchiectasis (Figs 8.46 and 8.54). None of these features is specific for asbestosis, and similar changes may be seen in other lung diseases such as IPF.[289] When CT scans of patients with asbestosis are compared with those of patients with IPF, patients with asbestosis have a higher prevalence of parenchymal bands, centrilobular nodules, and subpleural curvilinear lines, while the prevalence of traction bronchiolectasis and honeycombing is lower.[290,291] Copley et al[292] have recently

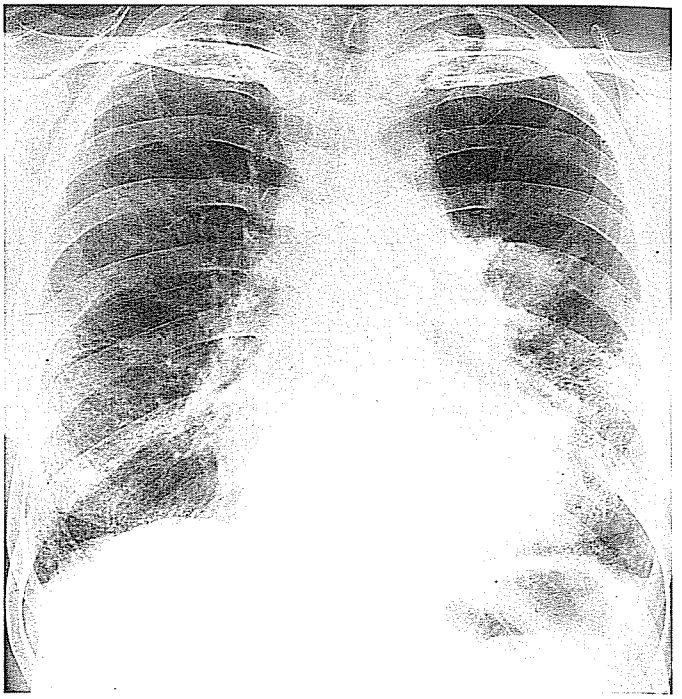

Fig. 8.52 Asbestosis with a bronchogenic carcinoma in the left lung. Note basal predominant fibrosis. There is slight blunting of the costophrenic sulci; otherwise, pleural changes are lacking in this case.

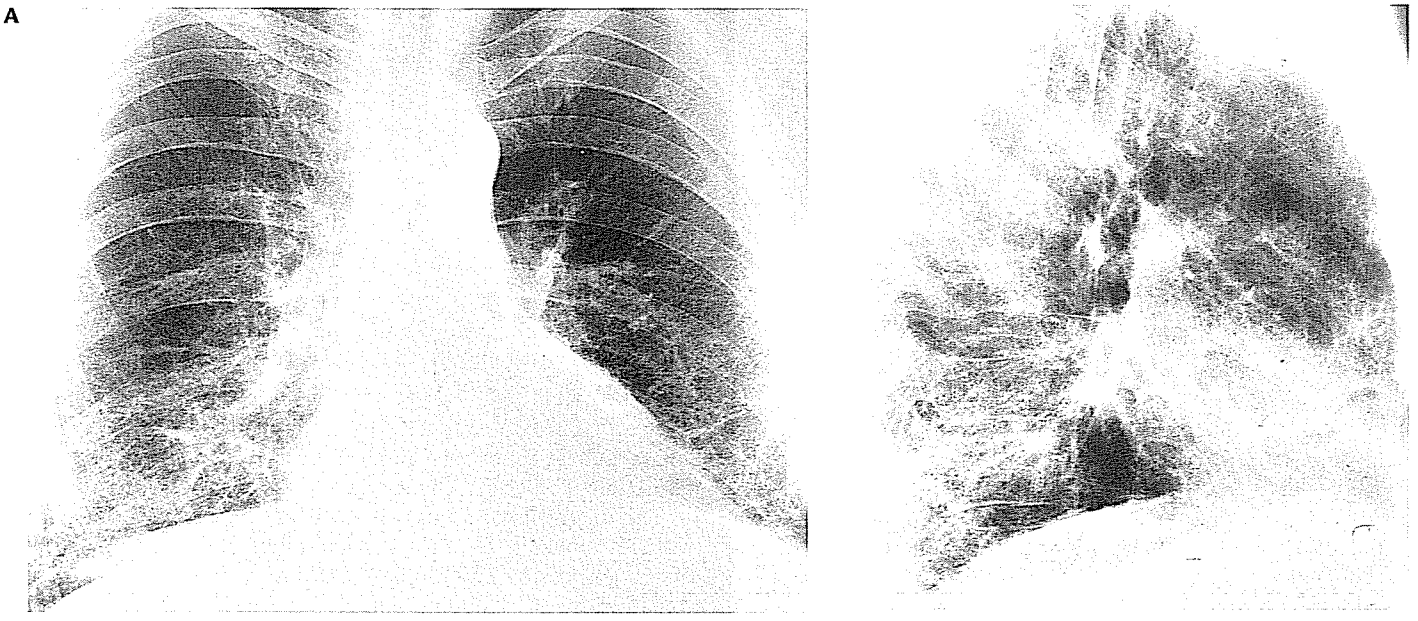

Fig. 8.51 **A**, Frontal and **B**, lateral radiographs of a shipyard worker with asbestosis showing basal predominant interstitial pulmonary fibrosis. There is widespread pleural calcification.

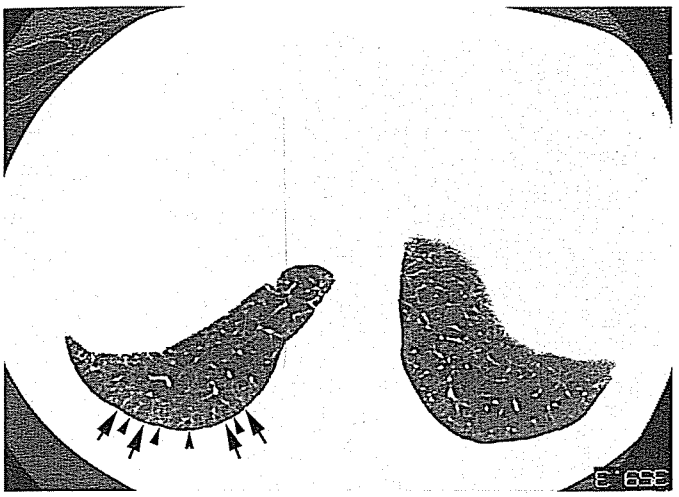

Fig. 8.53 Early asbestosis. Prone HRCT image shows posterior septal thickening (arrows) and centrilobular thickening (arrowheads). The changes were present bilaterally and at multiple levels.

shown that asbestosis shows a coarser pattern of fibrosis on CT than that found in UIP or NSIP.

The chest radiograph is relatively insensitive for detection of asbestosis[22,120,131,293] (Fig. 8.43). Staples et al[288] studied HRCT in asbestos exposed subjects with normal lung parenchyma on chest radiographs. Both vital capacity and diffusing capacity (percent predicted) were significantly lower in those who had abnormal HRCT scans. Similarly, in a study by Oksa et al,[294] an HRCT score for parenchymal abnormalities correlated significantly with diffusing capacity and total lung capacity in patients who had normal lung parenchyma on chest radiographs. Neri et al[295] showed that the presence of parenchymal abnormality on CT was associated with a significantly lower FVC in non-smoking asbestos exposed subjects. Thus, parenchymal abnormalities seen on CT in asbestos workers are clearly associated with physiologic impairment, even in those with normal chest radiographs.

The radiographic and CT changes of asbestosis usually progress over time, but the rate of progression is usually less than that seen in IPF. Akira et al[296] in a serial study of 23 asbestos exposed patients with minimal or no abnormalities on chest radiographs, demonstrated that the changes of early asbestosis progressed in two of seven patients who were reexamined between 10 and 19 months after the first CT scan, and in six of eight patients who were examined between 20 and 39 months after the first CT examination. This evidence of progression on CT was accompanied by decrease in lung diffusing capacity in three of four patients in whom serial pulmonary function tests were available. Progression of disease by HRCT criteria appeared to be more prominent in cigarette smokers. Using post mortem HRCT scans these authors also demonstrated that the centrilobular nodules and branching structures corresponded histologically to fibrosis around the bronchioles, which subsequently involved the alveolar ducts. Pleural based nodular irregularities corresponded histologically to subpleural fibrosis. Hazy patches of increased attenuation tended to correspond to fibrotic thickening of the alveolar walls and interlobular septa.

A study by Gamsu et al[297] shows that the CT findings of early asbestosis are neither sensitive nor specific. Some patients with abnormal lung parenchyma on CT have no histologic evidence of asbestosis, while some with normal CT or minor parenchymal abnormalities have histologic asbestosis. However, the study showed that asbestosis can be diagnosed with confidence when parenchymal changes are bilateral or present at multiple levels.

The relationship between asbestosis and lung cancer is controversial. Histologic asbestosis is almost invariably seen in asbestos workers who develop lung cancer.[131] Although there is a strong association between lung cancer and the presence of radiographic asbestosis[298,299] (Figs 8.55 and 8.56), asbestosis is not always visible on the chest radiograph or chest CT when lung cancer is present.[131,297,300,301]

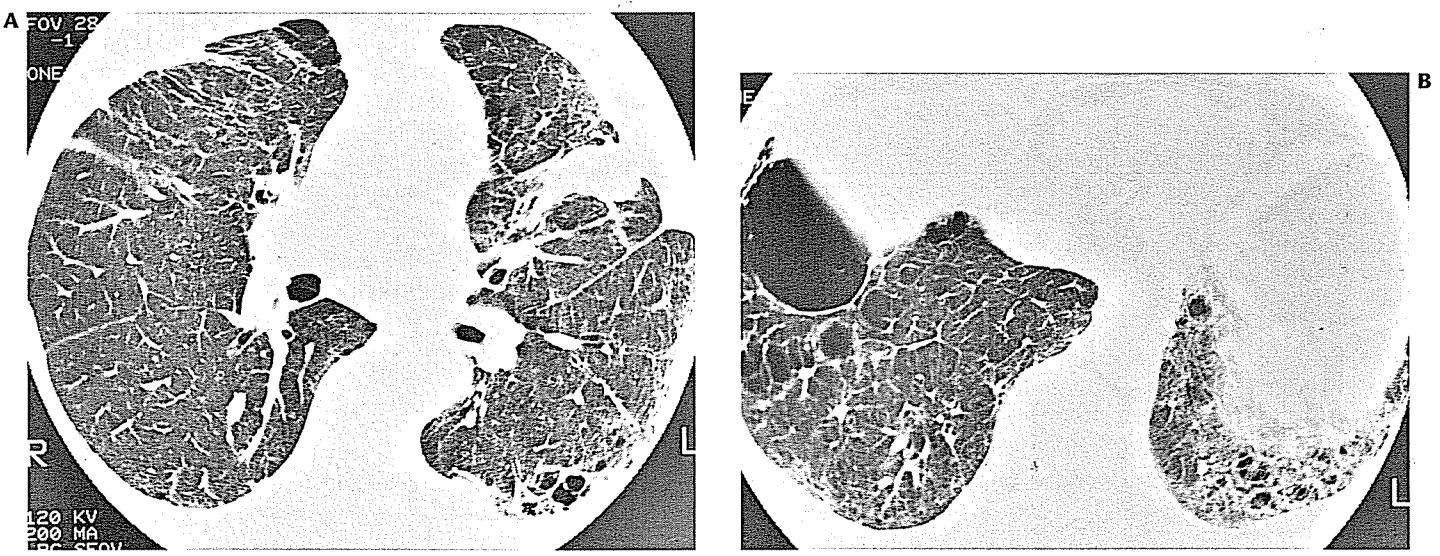

Fig. 8.54 Asbestosis. **A**, HRCT shows coarse bands of fibrous tissue extending into the lung from the pleural surface. Some of these bands emanate from a pleural plaque. **B**, HRCT at a lower level shows a right anterior bulla, with left basal reticular abnormality, traction bronchiectasis, and honeycombing. (Courtesy of Dr C Fuhrman, Pittsburgh)

foreign body (Fig. 8.83). These signs were seen in 20–45% of patients in the larger series.[358,360–362] A pneumothorax or a pneumomediastinum may be present, but both are surprisingly uncommon (<2% of patients) following aspiration of a foreign body.[358,362]

Normal inspiratory and expiratory chest radiographs can be expected in about one-quarter of cases. In the series of 200 patients reported by Blazer et al,[358] 15.6% of those with bronchial foreign bodies and 60.6% of those with tracheal foreign bodies showed no abnormalities on inspiratory and expiratory films. CT can be quite helpful in identifying the presence and location of an inhaled foreign body when inspiratory and expiratory radiographs are normal or equivocal, or when the diagnosis is not anticipated (Fig. 8.84).[366]

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